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December 5, 2001

Mr. Stephen Johnson  
Assistant Administrator  
U.S. Environmental Protection Agency  
Ariel Rios Building  
Room 3000, #1101-A  
1200 Pennsylvania Ave., N.W.  
Washington, DC 20460

Dear Mr. Johnson:

I hope this letter finds you well. I am writing on behalf of the 100,000 members of the Physicians Committee for Responsible Medicine (PCRM) interested in the development and regulatory acceptance of newer, more precise, nonanimal toxicity test methods.

I would like to tell you about an opportunity for the EPA to take a proactive step toward reducing the number of animals killed under its High Production Volume (HPV) Chemical Challenge. As you know, one of the six SIDS endpoints under the HPV program is ecotoxicity, which includes tests on algae, daphnia, and fish. This appears to be an appropriate time to replace the acute fish toxicity test with an established *in vitro* method for predicting aquatic toxicity.

On Tuesday, October 23, 2001, Sherry Sterling, Jessica Sandler of People for the Ethical Treatment of the Animals (PETA), and I coordinated a meeting at the EPA to facilitate incorporation of an *in vitro* aquatic toxicity test into the HPV program. We invited Terry Schultz, Ph.D., professor of predictive toxicology at the University of Tennessee College of Veterinary Medicine, to present his *in vitro* aquatic toxicity method, TETRATOX. TETRATOX has been standardized and has consistently yielded strong statistical agreement with the *in vivo* aquatic toxicity test. Where results from the two methods diverge, there are reasonable explanations. Overall, the extensive available information demonstrates TETRATOX to be a high quality surrogate for fish testing. In fact, this method is used extensively in private industry and is being considered for regulatory acceptance for a similar application by the Organization of Economic Cooperation and Development.

I was troubled to find that the EPA staff present at the meeting were not particularly interested in our contention that TETRATOX was ready for inclusion into the HPV program, because the attendees mainly deal with pesticide issues. TETRATOX is not

appropriate for pesticides, but it is entirely appropriate for industrial compounds, such as the HPV chemicals.

In a November 30, 2001, telephone conversation with Phil Sayre, Ph.D., associate director of the Office of Pollution Prevention and Toxics' Risk Assessment Division, Dr. Sayre stated that the EPA is not interested in the *in vitro* test because it provided no information on chronic toxicity. However, as you know, chronic fish toxicity is not an endpoint in the HPV program. As with all alternative methods, TETRATOX should be considered for the specific endpoint(s) for which it is appropriate, and not discounted because it cannot cover all possible endpoints. In this case, TETRATOX is an acceptable replacement of the acute fish toxicity screening test required under the HPV program.

In our October 17, 2001, meeting with you, you reaffirmed the EPA's commitment to animal welfare in the HPV program. One of the principles of the October 1999 Agreement reflects the EPA's expectation that nonanimal test methods for some SIDS endpoints may soon be available for replacement of the animal studies. To show good faith in the commitment made in the October 1999 Agreement, the EPA should actively pursue inclusion of nonanimal test methods wherever possible.

PCRM is concerned that large numbers of fish are being killed in the HPV program and other EPA programs, when established *in vitro* aquatic toxicity tests, such as TETRTOX, are available. Furthermore, some of the tests on fish that have been proposed are completely unnecessary given the physicochemical properties of some of the compounds.

- For example, under the HPV program thus far, the American Petroleum Institute proposed acute toxicity tests on fish with volatile substances such as the petroleum gases ethane, butane, isobutene, and propane.
- Three of the Flavor and Fragrance High Production Volume Consortia test plans called for fish toxicity tests with Generally Recognized As Safe chemicals including cinnamyl derivatives, which is essentially cinnamon oil.
- Fatty acids, including oleic, linoleic, stearic, and palmitic acids, have been proposed for fish tests. As you know, oleic acid is the main component of olive oil. Without a detergent or other additive, the olive oil will simply float at the top of the water. Moreover, detergents have toxic properties that make the results of these experiments questionable at best.
- Tests on fish have been proposed with corrosive chemicals that must first be neutralized to bring the pH to a level that will not kill the fish. Companies acknowledge that this changes the fundamental composition of the material and that such test conditions make the results meaningless. Nevertheless, they continue to propose and conduct the tests in order to "satisfy the EPA."

PCRM agrees with PETA that the EPA should take proactive steps in facilitating the incorporation of the TETRATOX assay into the HPV program. We request that the EPA

direct some of the \$500,000, which still has not been adequately accounted for, toward the sponsorship of the TETRATOX assay through the Science Advisory Board (SAB) or the Interagency Coordinating Committee on the Validation of Alternative Methods.

Specifically, we would greatly appreciate a response to the following questions:

- What is the extent of the EPA's interest in TETRATOX?
- Is the EPA's interest in using TETRATOX as a surrogate for the acute aquatic toxicity test in the HPV program compromised because it does not address chronic toxicity?
- Is TETRATOX a method that the EPA thinks has inter-agency applicability and therefore should be sponsored through ICCVAM? If so, is the EPA willing to use some of the \$500,000 to sponsor the test through ICCVAM? If not, is the EPA interested in reviewing TETRATOX through the SAB/SAP process?

Thank you for your consideration on this important matter. I look forward to your response. I can be reached at 202-686-2210, ext. 302, or at 5100 Wisconsin Ave., N.W., Suite 400, Washington, DC 20016.

Sincerely,

A handwritten signature in cursive script, reading "Nicole Cardello".

Nicole Cardello, M.H.S.  
Staff Scientist